DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Carlene Galligan
Associate Director, Drug Regulatory Affairs
Boehringer Ingelheim Pharmaceuticals, Incorporated
900 Ridgebury Road, PO Box 368
Ridgefield, CT 06877-0368

RE: NDA No. 21-395 Spiriva® HandiHaler® (tiotropium bromide inhalation powder)
NDA No. 20-579 Flomax® (tamsulosin hydrochloride) Capsules
NDA No. 20-667 Mirapex® (pramipexole dihydrochloride) Tablets
MACMIS ID #17308

Dear Ms. Galligan:

As part of its monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) of the U.S. Food and Drug Administration (FDA) has reviewed Boehringer Ingelheim Pharmaceuticals Incorporated's (Boehringer) sponsored links on internet search engines (e.g., Google.com) for the following products: SPIRIVA® HandiHaler® (tiotropium bromide inhalation powder) (Spiriva), Flomax® (tamsulosin hydrochloride) Capsules (Flomax), and Mirapex® (pramipexole dihydrochloride) Tablets (Mirapex). The sponsored links are misleading because they make representations and/or suggestions about the efficacy of Spiriva, Flomax, and Mirapex, but fail to communicate **any** risk information associated with the use of these drugs. In addition, the sponsored link for Flomax inadequately communicates the drug's indication. Furthermore, all of the sponsored links fail to use the required established name. Thus, the sponsored links misbrand the drugs in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and FDA implementing regulations. *See* 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

Background

Spiriva

According to its FDA-approved product labeling (PI), Spiriva is indicated for the long-term, once-daily, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

Spiriva is associated with a number of risks, as reflected in the Contraindications, Warnings, Precautions, and Adverse Reactions sections of its PI.

Flomax

According to its FDA-approved PI, Flomax is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH). Flomax is not indicated for the treatment of hypertension.

Flomax is associated with a number of risks, as reflected in the Contraindications, Warnings, Precautions, and Adverse Reactions sections of its PI.

Mirapex
According to its FDA-approved PI, Mirapex is indicated, among other things, for the treatment of moderate-to-severe primary Restless Legs Syndrome (RLS).

Mirapex is associated with a number of risks, as reflected in the Contraindications, Warnings (including bolded warnings), Precautions, and Adverse Events sections of its PI.

Omission of Risk Information

Promotional materials, other than reminder pieces, which include the name of the drug product but do not include indications or other representations or suggestions relative to the drug product (see 21 CFR 200.200, 201.100(f), 202.1(e)(2)(i)), are required to disclose risk and other information about the drug. Such materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The sponsored links present the following claims:

- Spiriva & COPD
  www.Spiriva.com Learn How Spiriva May Help You Manage Your COPD.

- Enlarged Prostate / BPH
  www.4Flomax.com Check Your Symptoms of BPH & Learn About Treating Prostate Problems.

- Mirapex ® Official Site
  www.Mirapex.com Treatment for Moderate To Severe Primary Restless Legs Syndrome.

These sponsored links make representations and/or suggestions about the efficacy of Spiriva, Flomax, and Mirapex, respectively, but fail to communicate **any** risk information. For promotional materials to be truthful and non-misleading, they must contain risk information in each part as necessary to qualify any claims made about the drug.

By omitting the most serious and frequently occurring risks associated with the drugs promoted in the links above, the sponsored links misleadingly suggest that Spiriva, Flomax, and Mirapex are safer than has been demonstrated. We note that these sponsored links contain a link to the products' websites. However, this is insufficient to mitigate the misleading omission of risk information from these promotional materials.

Inadequate Communication of Indication

The sponsored link for Flomax provides a very brief statement about what the drug is for; however, this statement is incomplete and misleading, suggesting that Flomax is useful in a

broader range of conditions or patients than has been demonstrated by substantial evidence or substantial clinical experience.

Specifically, the sponsored link for Flomax misleadingly broadens the indication for Flomax by implying that all patients with "prostate problems" are candidates for Flomax therapy ("Learn About Treating Prostate Problems"), when this is not the case. Rather, the only "prostate problem" Flomax is indicated for is the treatment of the signs and symptoms of BPH. Thus, the sponsored link misleadingly broadens the indication for Flomax.

Failure to Use Required Established Name

None of the sponsored links present the full established name of the drugs being promoted, despite the requirement to do so. *See* 21 CFR 201.10(g)(1) & 202.1(b)(1).

Conclusions and Requested Action

For the reasons discussed above, the sponsored links misbrand Spiriva, Flomax, and Mirapex, in violation of the Act and FDA regulations. *See* 21 U.S.C. 352(a) & (n), 321(n); 21 CFR 201.10(g)(1), 202.1(b)(1), (e)(3)(i), (ii) & (e)(6)(i).

DDMAC requests that Boehringer immediately cease the dissemination of violative promotional materials for Spiriva, Flomax, and Mirapex, such as those described above. Please submit a written response to this letter on or before April 9, 2009, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) in use for these drugs as of the date of this letter, identifying which of these materials contain violations such as those described above, and explaining your plan for discontinuing use of such materials. Finally, we encourage you to review your promotional materials for the other prescription drug products that Boehringer promotes in the United States and to discontinue or revise any materials with the same or similar violations, and request that your response address this issue as well.

Please direct your response to the undersigned at the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising, and Communications, 5901-B Ammendale Road, Beltsville, MD, facsimile at 301-847-8444. In all future correspondence regarding this matter, please refer to MACMIS # 17308 in addition to the NDA numbers. We remind you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Spiriva, Flomax, and Mirapex comply with each applicable requirement of the Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Shefali Doshi, M.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Shefali Doshi

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